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1 **Cluster randomised controlled trial of a nurse-led psychological intervention for type 2**
2 **diabetes: Diabetes-6 study**

3

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13

15 **Abstract**

16 **Background**

17 Suboptimal glycaemic control in type 2 diabetes (T2D) is common and associated with
18 psychological barriers.

19 **Aim**

20 We tested whether it was possible to train practice nurses in six psychological skills
21 (Diabetes 6 (D6)) based on motivational interviewing (MI) and basic cognitive behaviour
22 therapy (CBT) and whether integrating these with diabetes care was associated with
23 improved glycaemic control over 18 months compared to standard care.

24 **Design and Setting**

25 A two-arm, single-blind, parallel cluster randomised controlled trial conducted in primary
26 care practices (n=24) (ISRCTN trial registration: ISRCTN75776892).

27 **Method**

28 Adult participants (n=334) with T2D and HbA1c ≥ 69.4 mmol/mol (lowered to ≥ 64
29 mmol/mol midstudy to increase recruitment) at least once in previous 18 months and at
30 recruitment were randomised to receive 12 sessions of either the D6 intervention or standard
31 care over 12 months. The practice nurses were trained in the six psychological skills and
32 their competencies were measured by standardised rating scales. All sessions were
33 audiotaped. The primary outcome was change in HbA1c at 18 months from randomisation;
34 secondary outcomes were change in systolic and diastolic blood pressure, body mass index,
35 waist circumference, depressive symptoms, harmful alcohol intake, diabetes-specific distress,
36 and cost-effectiveness.

37

38 **Results**

39 Using intention-to-treat analysis, there was no significant difference between D6 intervention
40 and standard care in HbA1c (absolute mean difference -0.79 mmol/mol, 95% CI -5.75–4.18)
41 or for any of the secondary outcomes. The competency level of D6 nurses was below the
42 beginner proficiency level and similar to the standard care nurses.

43 **Conclusion**

44 Training nurses in MI and basic CBT to support self-management did not lead to
45 improvements in glycaemic control or other secondary outcomes in people with T2D at 18
46 months. It was also unlikely to be cost-effective. Furthermore, the increased contact with
47 standard care nurses did not improve glycaemic control.

48
49 **Keywords:** Type 2 diabetes, Self-management, Motivational interviewing, Cognitive
50 behavioural therapy, Glycaemic control

52 **How this fits in**

53 The evidence that low intensity psychological interventions to support self-management in
54 people with poorly controlled type 2 diabetes in primary care setting is limited.

55 It is not known whether practice nurses can be trained to deliver low intensity psychological
56 treatments to support self-management in type 2 diabetes.

57 Training on low intensity psychological interventions based on motivational interviewing and
58 basic cognitive behaviour therapy led to basic proficiency in these skills but this was not
59 maintained.

60 Offering more sessions with practice nurses to support self-management in people with
61 persistent hyperglycaemia does not lead to improvement in glycaemic control in type 2
62 diabetes.

63

64 **Introduction**

65 Around half of people with type 2 diabetes (T2D) have persistent suboptimal glycaemic
66 control despite evidence based pathways based on national guidance.¹⁻³ Psychological
67 factors, such as depressive symptoms and diabetes-specific fears are common in T2D and
68 associated with reduced self-management.^{4,5} Addressing these psychological barriers could
69 lead to improvement in glycaemic control.

70 Common psychological interventions include motivational interviewing (MI)⁶ and cognitive
71 behaviour therapy (CBT).^{7,8} Recent randomised controlled trials (RCT) suggest that the
72 effect of low-intensity psychological interventions on glycaemic control is lower than
73 reported in systematic reviews.⁹⁻¹¹

74 One of the roles of the practice nurse is to support diabetes self-management. Hospital
75 diabetes specialist nurses can be trained to competently deliver MI and basic CBT skills with
76 improvement in glycaemic control in type 1 diabetes¹² and psychological interventions could
77 be delivered by nurses in research settings.¹³ We defined a package of six psychological
78 skillsets for T2D (Diabetes 6 (D6)) of similar intensity to low-level psychological treatments
79 for common mental disorders in the NHS.¹⁴ We tested in a cluster RCT whether training
80 practice nurses in D6 skills was associated with increased competency than nurses not receive
81 the training, and whether the D6 intervention was more effective than standard care in
82 improving suboptimal glycaemic control in people with T2D over 18 months and in
83 improving secondary outcomes (such as lipids, depressive symptoms), and if it was cost-
84 effective.

85 **Method**

86 **Trial design**

87 D6 was a pragmatic parallel two-arm cluster RCT design for 18 months. GP practices with
88 ≥ 6000 patients registered in the Lambeth, Southwark, Lewisham, Wandsworth, and Bexley
89 Clinical Commissioning Groups (representing a resident population of 1.43 million), were
90 invited to participate if they had a practice nurse delivering diabetes care. Recruitment of
91 patients began after each practice consented to randomisation. Randomisation of clusters was
92 conducted in two phases, as recruitment of practices and patients had slowed down following
93 the organisational uncertainties preceding the implementation of the Health and Social Care
94 Act 2012. This Act re-organised the UK's National Health Service (NHS), dismantling
95 current organisational structures and creating new ones for funding, management,
96 accountability and regulation.¹⁵

97 **Patients**

98 Inclusion criteria were: adults aged 18–79 years, duration of T2D for ≥ 2 years, persistent
99 suboptimal glycaemic control defined as International Federation of Clinical Chemistry
100 (IFCC) HbA1c ≥ 69.4 mmol/mol (National Glycohemoglobin Standardization Program
101 (NGSP) 8.5%) on two occasions (at least once in the preceding 18 months and the second one
102 at recruitment) while on at least two oral diabetes medication (metformin and one other),
103 and/or requiring insulin therapy to ensure that efforts to optimise medical care had been
104 offered to the patient.¹⁵ The IFCC HbA1c was lowered to ≥ 64 mmol/mol (NGSP 8%) in
105 Phase 2 to increase recruitment.

Exclusion criteria were: severe mental disorders; terminal illnesses and end-stage diabetes complications; morbid obesity (body mass index (BMI) >40 kg/m² in Phase 1 and >50 kg/m² in Phase 2); non-ambulatory; no phone/internet access; non-English-speaking; and receiving psychological treatments elsewhere. Patients who had Patient Health Questionnaire-9 (PHQ-9) depressive scores >20 were excluded if they had psychotic depression or active suicidal ideation.¹⁶

Baseline measures

Baselines measures before randomisation were: age, gender, self-reported ethnicity, occupation, employment status, and smoking status. Complication status included: neuropathic ulcer risk by perception of 10g monofilament; retinopathy coding of the most recent annual standardised digital retinal photography; nephropathy using the urinary albumin:creatinine ratio (ACR); and history of macrovascular complications.

Randomisation

Randomisation of practices (unit of cluster) was conducted by an independent statistician using a random number generator to assign equal numbers of practices to each arm at each phase. For allocation concealment, an independent manager held the randomisation list in password-locked computer.

Intervention

Group 1: Standard care

The nurse delivered diabetes care in both groups as recommended by national guidance, which included diabetes self-management education, monitoring of biomedical status, and giving clinical information and advice.¹⁷ To control for attention, standard care nurses offered the same number of sessions as D6. This consisted of 12 sessions, each 30 minutes in duration, over 12 months. The sessions were held in routine primary care clinics and audiotaped.

Group 2: Standard care plus Diabetes 6

The theory underlying MI is that the patient's state of ambivalence (resistance versus willingness to make lifestyle changes) is the core psychological construct that needs addressing.⁶ MI is a directive, counselling style which encourages patients to change behaviours using collaborative, non-judgmental, and affirming communications. The theory underlying CBT is that barriers to diabetes self-management are maintained by unhelpful thoughts (e.g., *if I can't cure diabetes, what's the point?*), unhelpful behaviours (e.g., missing insulin doses), and distressing emotions (e.g., low mood/anxiety when seeing a high blood glucose reading).^{18,19} Identifying and challenging these cognitive barriers are effective in changing behaviours.²⁰ The D6 nurses were trained to integrate diabetes care with six skills drawn from MI and CBT, as follows : 1. Active listening; 2. Managing resistance; 3. Directing change; 4. Supporting self-efficacy; 5. Addressing health beliefs; and 6. Shaping behaviours. This consisted of 12 sessions, each 30 minutes in duration, over 12 months. The sessions were held in routine primary care clinics and were audiotaped.

146 The Motivational Interviewing Treatment Integrity (MITI) Scale (version 3.1.1)²¹ and
147 Behaviour Change Counselling Index (BECCI)²² were used to compare competencies in both
148 groups. The middle 20 minutes of sessions were rated by two independent psychologists
149 trained in MITI and the BECCI was rated by a clinical psychologist, blind to treatment
150 allocation.

151 **Outcomes**

152 The follow-up was reduced from 24 to 18 months secondary to the delays in recruitment. The
153 primary outcome was change in HbA1c (mmol/mol) from cluster randomisation to 18 months
154 measured centrally (King's College Hospital NHS Foundation Trust) by affinity
155 chromatography (Primus Ultra2, Kansas City, USA). If the study HbA1c were missing at 18-
156 month, we included the 15-month HbA1c as this clinically overlaps with the 3-month
157 window for 18-month HbA1c. The following secondary outcomes were change in systolic
158 and diastolic blood pressure using an electronic sphygmomanometer; BMI, and waist
159 circumference (cm); depressive symptoms using the PHQ-9;¹⁶ the Alcohol Use Disorders
160 Identification Test (AUDIT);²³ and the Diabetes Distress Scale, which measures diabetes-
161 specific psychological burden.²⁴ A fasting blood sample was used for HbA1c, total
162 cholesterol, and triglycerides.

163 **Sample size**

164 An IFCC HbA1c 10.9 mmol/mol (NGSP HbA1c 1%) difference in D6 compared to standard
165 care was the minimal clinically significant reduction at 18 months, considering that standard
166 care may produce a 2.2 mmol/mol (NGSP HbA1c 0.2%) reduction in HbA1c (equivalent to a
167 moderate effect size of $d=0.55$). Assuming 20% dropout, we needed 360 patients to achieve

168 80% power at a two-sided alpha-level of 5%, with 20 practices with 18 patients each per arm.
169 We assumed two practices per arm would dropout, thus requiring 24 practices with a total
170 patient sample of $24 \times 18 = 432$ patients. After adjusting for clustering by practice (clustering
171 intra-correlation coefficient (ICC)=0.05) and an inflation factor of 1.7, the final required
172 sample size was $81 \times 1.7 = 138$ patients per arm.

173 We recruited 334 patients of which 231 had at least one follow-up in 24 clusters. The average
174 cluster size was therefore 10 patients per cluster, smaller than our assumed size of 15 patients
175 per cluster with a post-hoc power of 77% at two-sided alpha-level of 5%.²⁵

176 **Statistical analysis**

177 Data were analysed using STATA 13. The sample characteristics were described as means
178 (standard deviation (SD)) or as proportions (percentage). A comparison of patient list size
179 and Index of Multiple Deprivation (IMD) 2010 rank score by practices that participated
180 versus those that did not was conducted using Student's t-test. The IMD 2010 score is a
181 composite index of relative deprivation at a small area level, based on seven domains of
182 deprivation: income, employment, health deprivation and disability, education, skills and
183 training, barriers to housing and services, crime and disorder, and living environment.²⁶ A
184 linear mixed-effects model estimated group differences in HbA1c levels between D6 and
185 standard care groups at 18 months. Nurse was included as a random effect as the unit of
186 randomisation. Secondary outcomes were also analysed using linear mixed models to
187 estimate group differences at 18 months.

188 Twenty-nine participants with HbA1c < 64 mmol/mol were mistakenly recruited because of
189 coding errors by the research team during assessment of eligibility and this mistake was only

discovered after randomisation. Therefore, they were retained for the ITT. We performed a sensitivity analysis by including a binary covariate of this protocol violation using maximum likelihood under the missing at random assumption. Sensitivity to missingness in HbA1c was assessed by investigating and including predictors of missingness in the model and by using multiple imputation for the missing values of HbA1c.

For further details of the protocol, including the economic evaluation, see Appendix 1.

Results

We invited 116 practices, 26 agreed to participate and two dropped out before randomisation (Figure 1; Appendix2:Table 1) and 995 potentially eligible participants. Of the 451 who consented for eligibility, 334 were recruited. Twelve practice clusters were randomly assigned to standard care (n=164 participants) and 12 to standard care plus D6 (n=170). One D6 practice dropped out after randomisation, before the nurse received the training, and before all patients were recruited (those who consented remained in the ITT analysis). Invited practices that participated (n=24) compared to those that did not (n=89) had higher mean patient list sizes (12180 (SD=5099) vs. 10091 (SD=3894), $p=0.03$) but no difference in IMD score (10049 (SD=6910) versus 12441 (SD=7785), $p=0.17$). Table 1 presents the baseline characteristics of the sample.

Figure 1 here; Table 1 here

The mean number of sessions attended was 7.42 (SD=4.4) and 8.20 (SD=4.4) in the D6 and standard care groups, respectively.

Primary outcome data at 18-month follow-up were collected for 219 (65.6%) participants and a further 12 had 15-month HbA1c data, providing 231 participants. There was a non-significant larger proportion with missing HbA1c in the D6 group compared to standard care (35.9% versus 32.9%, respectively) (Appendix 2:Table 2) and more likely to be African/Caribbean or Asian/Other ethnicity. In the ITT analysis, there was no significant difference in mean HbA1c at follow-up in the D6 group compared to the standard care group (table 2). The ICC for the clustering effect of nurse was 0.02 (95% CI 0.001–0.37). Linear mixed models showed no significant effects of the intervention on the secondary outcomes including BMI, blood pressure, fasting triglyceride, or psychological distress (table 2).

Table 2 here

Results were similar for the sensitivity analyses when: using practice as the clustering variable in place of nurse as cluster; including a binary covariate for the 29 participants with baseline HbA1c <64 mmol/mol; including ethnicity and history of stroke as predictor of missingness at follow-up; or using multiple imputation to account for missingness in HbA1c (Appendix 2:Table 2). There was no evidence of an association between the number of D6 sessions attended and HbA1c at 18 months within the D6 group (-0.44 mmol per additional session attended, 95% CI -1.28–0.41).

Intervention costs were higher in the D6 group (mean difference £276, 95% CI £225–£327) (Table 3) due to greater training costs but there were no differences in mean total health and social care costs (adjusted mean difference £150, 95% CI -£34–£333) or QALY gains at 18 months (Appendix 4).

Table 3 here

The inter-rater reliability for the MITI global domains of spirit and empathy was 0.87 and 0.91 respectively so we combined both sets of ratings and derived the mean score for each domain. We rated 69 sessions (4.0% of all available recordings) for fidelity from 33/170 and 36/164 patients from the D6 and standard care groups respectively (Table 4). The level of competency in the D6 group was below the beginner proficiency level in all the scales for MI and BECCI. Except for a slightly higher proportion of open questions in D6, and a slightly larger reflection/question ratio in standard care, there were no statistically significant differences in the remaining mean MI domain scores or BECCI scores.

Table 4 here

There were 43 serious adverse events (cardiovascular (n=11), injury (n=5), cancer (n=4), infection (n=5), diabetes-related (n=3), psychiatric (n=2), and other (n=10)), reported after 18 months for 38 different participants (D6 n=14; standard care n=24) and 2 deaths from cancer, with no difference between the two groups

Discussion

Summary

Training nurses in MI and basic CBT to support self-management did not lead to improvements in glycaemic control, or any other secondary outcomes, in people with T2D and persistent hyperglycaemia compared to attention control at 18 months from randomisation. Further, it was unlikely to be cost-effective.

Strengths and limitations

252 This was a pragmatic design set in real-world, inner-city, primary care representing the ethnic
253 and social diversity of people with T2D.²⁷ Only a few other RCTs have achieved similar
254 ethnicity distributions.^{28–34} This was a high risk group for diabetes complications. We
255 selected a cluster design to reduce contamination of the intervention in the control group.
256 Contamination is the process whereby an intervention intended for members of the trial
257 (intervention or treatment) arm of a study is received by members of another (control) arm
258 leading to a risk of under estimation of the effect.³⁵ We assessed contamination by comparing
259 the competencies in the intervention and control group. The hypothesis was that the control
260 group would have lower competencies than the D6 group. As both groups had similar and
261 borderline beginner proficiency competencies (which is probably the pre-training level of
262 competency) we concluded it was unlikely there was contamination. We developed a
263 theoretically informed intervention and an evidence-based manual. We measured fidelity
264 (which is the same measure as competency in this study) to the intervention. We controlled
265 for the non-specific effect of receiving more attention by D6 by offering similar number of
266 sessions to patients randomised to the control group. We were only slightly underpowered at
267 77% power compared to the 80% originally proposed. The upper limit of the 95% confidence
268 interval of the estimated treatment effect for HbA1c (4.8 mmol/mol) was less than estimated
269 treatment reductions in meta-analyses.³⁶ The comprehensive within-trial economic evaluation
270 assessed all relevant health and social care costs.

271 The limitations of D6 included a 20% uptake of practice participation, despite the offer of
272 generous backfill payments. The main reasons given by the practices when feedback was
273 informally asked were the pressures to deliver current services with limited resources
274 exacerbated by co-incidental national restructuring of primary care services creating
275 organisational uncertainty. Data missingness for the economic analyses was high, however,

imputing missing data confirmed the lack of cost-effectiveness of D6. We did not obtain sufficient repeated measures of HbA1c. We failed to achieve a minimum level of beginner proficiency in motivational interviewing in the D6 group therefore unable to conclude that motivational interviewing is not effective in supporting self-management.

Comparison with existing literature

Although there have been over 40 RCTs in this field since the last review,³⁶ only three had defined poor glycaemic control (HbA1c ≥ 64 mmol/mol) as an inclusion criterion and showed no benefit from psychological support and only one of these was delivered by nurse care managers.^{37–39} Recent pragmatic RCTs of similar interventions included samples with near optimal glycaemic control with less room for improvement in the primary outcome.^{10,11,40} Our sample had sustained high HbA1c so we may have selected a more severe group not suitable for practitioners with lower levels of psychological skill competencies.^{28–34}

We are one of a handful of RCTs to include fidelity and competency (a complex, laborious, and expensive process evaluation).^{41,42} On average patients attended only 50% of sessions in either group. This is a common observation in psychological interventions.⁴³ However, no dose-response relationship was observed.

Implications for research and/or practice

There are several potential nurse, patient and methodological reasons for the non-significant effect of D6. The nurses did not self-select and may not have had the generic psychotherapist factors often attributed as the active ingredients in psychological treatments.⁴⁴ D6 nurses had concerns about over-stepping their professional roles, lacking confidence, and/or resented the

extra workload.⁴⁵ The low competencies in most MI and CBT domains suggest that practice nurses may need longer periods of training or should self-select for generic psychotherapist skills in advance. Our findings may also reflect the difficulty of engaging this high risk clinical group but with low levels of worry. Even offering more nurse support in the form of more frequent sessions did not lead to improved glycaemic control. In exit interviews, patients stated they lacked time (although the majority was not employed) and difficulties in establishing a rapport with the nurses as reasons for dropout (unpublished observations). One methodological explanation is that we selected HbA1c, strongly associated to the levels of glycaemia, as a surrogate outcome for diabetes complications. However, a landmark RCT⁴⁶ and a meta-analysis of RCTs⁴⁷ aimed at intensive glycaemic control have failed to observe consistently a positive effect on reduction of complications of diabetes or global mortality and there may be even a negative effect of increased mortality when tight glycaemic control is the aim. Perhaps these negative findings represent an opportunity to focus on psychological interventions to improve other outcomes such as blood pressure, lipids or a composite outcome. Another methodological implication is whether the duration of the intervention and the follow up was too short. Brief psychological interventions are designed to be exactly that, with the added advantage of being cheap and not too demanding on the patient. However, our patients had a long history of poor self-management and may have needed a longer duration of therapy. Whether longer therapy would be pragmatic to be funded as a RCT or in the NHS is to be debated and is showing promise for chronic depression.⁴⁸

The implication for clinical practice is that low-intensity psychological interventions delivered at low level of competencies may not be as effective in supporting self-management in people with T2D and longstanding suboptimal glycaemic control as previously thought.

321

322 A conceptual dilemma is that theoretical frameworks for MI and CBT assume that mental
323 health conditions remit (alcohol problems, smoking, depression) and this assumption does not
324 apply to T2D which progressively worsen.⁴⁹

325 We urgently need to reconsider what skills, what competencies, which workforce are the
326 most effective in delivering psychological interventions to improve glycaemic control in
327 people with T2D⁵⁰ before investing sparse funds into low intensity psychological treatments
328 for improving glycaemic control in T2D.⁵¹

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353 **Author Contributions**

354 KI, SAA, DStahl, AP, SMT developed the hypotheses. SAA and KI led the conduct of the
355 study; KW project managed and contributed to analysis, training and assessment of nurses;
356 NDZ developed the Diabetes 6 manual, the protocol for fidelity and did the training and
357 supervision of the nurses; DStahl was the senior trial statistician and led the statistical plan
358 and DStringer conducted the statistical analysis; AP designed and led the economic
359 evaluation and MH conducted the economic analysis. KI drafted the manuscript and all
360 authors contributed to the drafts and approved final version.

361 **Competing Interests**

362 All authors have completed the ICMJE uniform disclosure form at
363 www.icmje.org/doi_disclosure.pdf. KI has received honorarium from Eli-Lilly, Sanofi,
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Ethical Approval

Ethical approval was granted by the King's College Hospital Research Ethics Committee (reference 09/H0808/97) and Primary Care Trusts (references RDLSLBex 534 and 2010/403/W). Changes to the protocol were approved by the Trial Steering Committee and the Research Ethics Committee. All participants gave written, informed consent and the trial was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki.

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The corresponding author (KI) had full access to all the data in the study and had final responsibility for the decision to submit for publication. We attest that we have obtained appropriate permissions and paid any required fees for use of copyright protected materials.

Data Sharing

The protocol and patient-level data are available from the corresponding author upon request.

396

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Figures

Figure 1. Diabetes 6 (D6) study flow chart

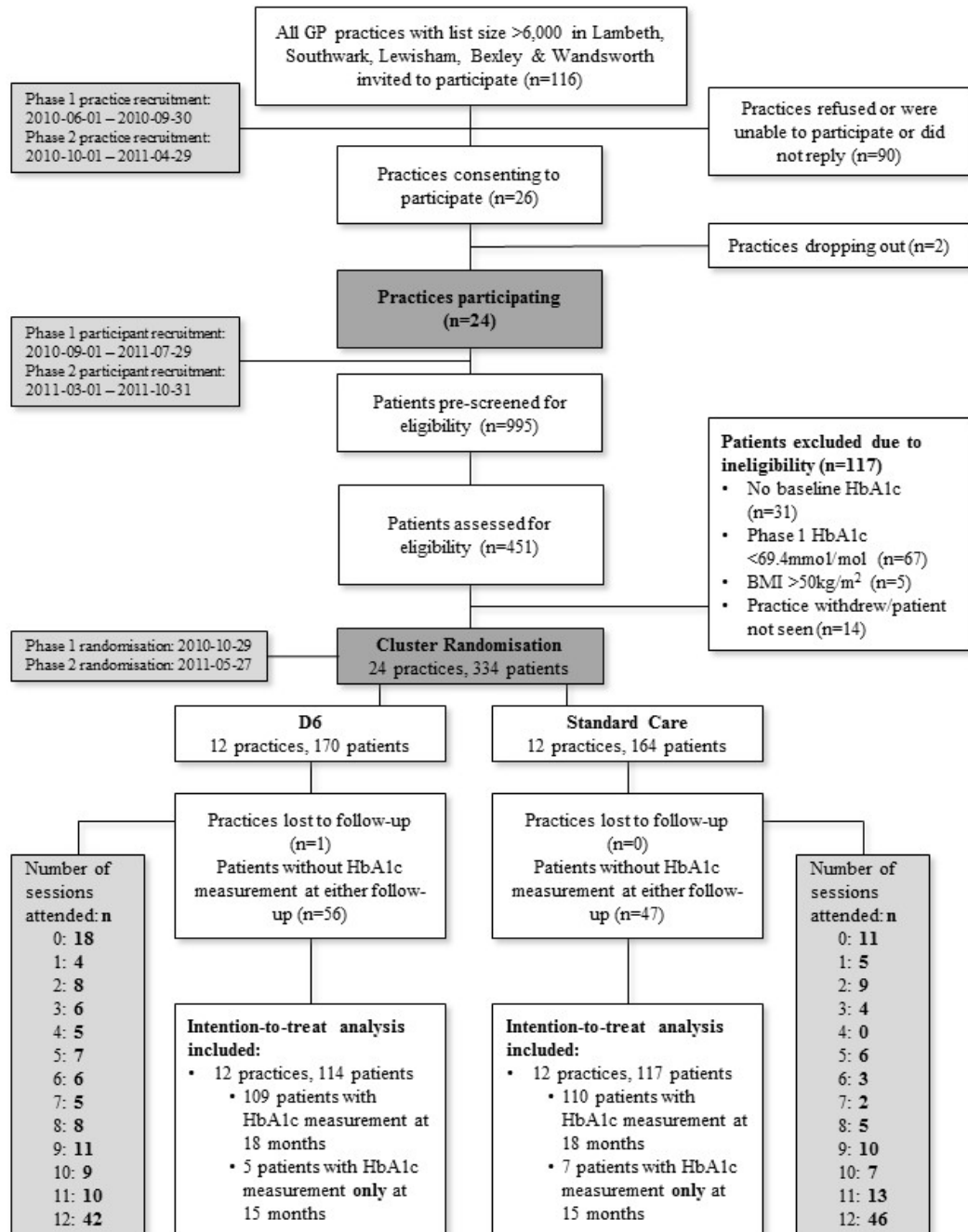


Table 1. Baseline characteristics of participants randomly assigned to receive D6 or standard care.			
Variable*	D6 (n=164)	Standard Care (n=170)	Total
Age (years)	59.0 (11.1)	58.9 (11.4)	58.9 (11.2)
Gender			
Male	82 (50.0%)	81 (47.7%)	163 (48.8%)
Female	82 (50.0%)	89 (52.4%)	171 (51.2%)
Ethnicity			
White	60 (36.8%)	74 (43.8%)	134 (40.4%)
African/Caribbean	81 (49.7%)	62 (36.7%)	143 (43.1%)
Asian/Other	22 (13.5%)	33 (19.5%)	55 (16.6%)
Relationship status			
Married or Cohabiting	82 (50.3%)	89 (52.7%)	171 (51.5%)
Separated/Divorced/Widowed	52 (31.9%)	45 (26.6%)	97 (29.2%)
Single	29 (17.8%)	35 (20.7%)	64 (19.3%)
Education level			
A-level or higher	47 (29.2%)	43 (25.8%)	90 (27.4%)
O-level or GCSE equivalent	68 (42.2%)	48 (28.7%)	116 (35.4%)
No formal qualifications	46 (28.6%)	76 (45.5%)	122 (37.2%)
Employment			
Yes ¹	69 (42.1%)	70 (41.2%)	139 (41.6%)
No ²	95 (57.9%)	100 (58.8%)	195 (58.4%)
Borough			
Lambeth	83 (50.6%)	42 (24.7%)	125 (37.4%)
Southwark	25 (15.2%)	40 (23.5%)	65 (19.5%)
Lewisham	19 (11.6%)	52 (30.6%)	71 (21.3%)
Wandsworth	37 (22.6%)	24 (14.1%)	61 (18.3%)
Bexley	0 (0.0%)	12 (7.1%)	12 (3.6%)
Diabetes duration (years)	10 (7–13)	9 (5–12)	9 (6–12)
HbA1c (mmol/mol)	81.0 (17.1)	80.1 (19.1)	80.5 (18.1)
Body mass index (kg/m ²)	32.0 (5.6)	31.9 (6.6)	31.9 (6.1)
Systolic blood pressure (mm/Hg)	135.2 (16.9)	133.2 (17.3)	134.2 (17.1)
Diastolic blood pressure (mm/Hg)	79.5 (9.8)	79.0 (10.3)	79.2 (10.1)
Total cholesterol (mmol/L)	4.3 (1.1)	4.2 (1.2)	4.2 (1.2)
Fasting triglycerides (mmol/L)	1.7 (1.2)	1.7 (1.3)	1.7 (1.3)
Taking insulin			
Yes	75 (46.3%)	66 (39.8%)	141 (43.0%)
No	87 (53.7%)	100 (60.3%)	187 (57.0%)
Any retinopathy			
Yes	59 (35.9%)	65 (38.2%)	124 (37.1%)
No	105 (64.0%)	105 (61.8%)	210 (62.9%)
Albumin:Creatinine ratio			

Negative	65 (59.1%)	83 (69.8%)	148 (64.6%)
Positive	45 (40.9%)	36 (30.3%)	81 (35.4%)
Protein:Creatinine ratio			
Negative	33 (76.7%)	17 (77.3%)	50 (76.9%)
Positive	10 (23.3%)	5 (22.7%)	15 (23.1%)
Foot ulcers			
Yes	9 (5.6%)	12 (7.1%)	21 (6.4%)
No	152 (94.4%)	157 (92.9%)	309 (93.6%)
Macrovascular disease			
Yes	61 (37.2%)	55 (32.4%)	116 (34.7%)
No	103 (62.8%)	115 (67.7%)	218 (65.3%)
Patient Health Questionnaire-9 score			
≥10	31 (20.4%)	35 (22.4%)	66 (21.4%)
<10	121 (79.6%)	121 (77.6%)	242 (78.6%)
Diabetes Distress Scale (mean item score)	2.1 (1.7–2.7)	2.0 (1.6–2.7)	2.1 (1.6–2.7)
<p>Data are n (%), median (IQR), or mean (SD), as appropriate.</p> <p>¹Yes = full-time, part-time, student or self-employed; ²No = retired/unemployed/not seeking employment</p> <p>*Values missing for age (n=1), ethnicity (n=2), relationship status (n=2), education level (n=6), diabetes duration (n=20), body mass index (n=5), systolic blood pressure (n=25), diastolic blood pressure (n=26), HbA1c (n=1), total cholesterol (n=53), fasting triglycerides (n=58), insulin (n=6), albumin:creatinine ratio (n=105), protein:creatinine ratio (n=269), foot ulcers (n=2), Patient Health Questionnaire-9 (n=26), diabetes distress scale (n=27).</p>			

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Table 2. Results from primary and secondary outcomes.			
Outcome at 18 months	Participants with baseline measurements	Participants with measurements at 18 months	Estimated Mean Difference: D6 vs standard care (95% CI)
Primary			
HbA1c (mol/mmol)*	332	231	-0.79 (-5.75–4.18)
Secondary			
Body mass index (kg/m²)*	329	152	-0.08 (-1.12–0.97)
Total cholesterol*	281	140	-0.08 (-0.42–0.27)
Systolic blood pressure (mm/Hg)*	309	198	-1.35 (-6.85–4.14)
Diastolic blood pressure (mm/Hg)*	308	198	1.22 (-1.87–4.32)
Fasting triglycerides**	276	135	0.02 (-0.22–0.26)
Patient Health Questionnaire-9 Score***	308	114	-0.18 (-1.30–0.94)
<p>*Estimates based on linear combination from linear mixed-effects model with fixed effects of time (15 or 18 months), an interaction between time and randomisation group, randomisation phase, borough and baseline values of the outcome, a random effect for GP practice nurse clustering and with unstructured covariance matrix to account for dependency of repeated observations.</p> <p>**Estimates based on linear combination from linear mixed-effects model with fixed effects of time (15 months or 18 months), an interaction between time and randomisation group, randomisation phase, borough and baseline values of the outcome, a random effect for GP practice nurse clustering and with independent covariance structure due to convergence issues when estimating non-zero covariances.</p> <p>***Collected at 18 months only. Estimates based on linear combination from linear mixed model with fixed effects of randomisation phase, borough, baseline value and random within-cluster effect of nurse with unstructured covariance matrix to account for dependency of repeated observations.</p> <p>D6=Diabetes 6</p>			

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Table 3. Mean costs (for the previous 6 months, £ sterling, 2011/12 prices), SF-12-based utility scores and QALY gains at baseline and/or 18 months.										
Costs at baseline	D6			Standard care			UMD*	95% CI	AMD**	95% CI*
	<i>valid n</i>	<i>Mea n £</i>	<i>SD</i>	<i>valid n</i>	<i>Mea n £</i>	<i>SD</i>				
Health and social care costs	157	847	847	161	976	760	-129	-301–44	-96	-293–101
Costs at 18 months										
Health and social care costs, excluding intervention, without discounting	133	707	579	137	793	558	-85	-252–81	-71	-242–100
Health and social costs, excluding intervention, with discounting	133	684	560	137	766	540	-82	-243–78	-69	-234–96
Intervention costs	121	451	99	139	167	100	285	240–329	276	225–327
Health and social care costs, including intervention costs, with discounting for non-intervention costs	92	1184	572	107	1025	573	159	-39–357	150	-34–333
SF-12-based utility scores at baseline										
Utility	157	0.75	0.16	159	0.74	0.16	0.01	-0.03–0.04	0.01	-0.03–0.00
SF-12-based utility scores and QALY gains at 18 months										
Utility	60	0.79	0.13	53	0.75	0.13	0.04	-0.01–0.08	0.01	-0.03–0.06
QALY gain since baseline, without discounting	58	1.15	0.20	48	1.11	0.18	0.03	-0.04–0.10	0.01	-0.03–0.05
QALY gain since baseline, with discounting and interpolation to match 6-month period for cost data	58	0.37	0.06	48	0.36	0.06	0.01	-0.01–0.03	0.00	-0.01–0.02
SF-12 = Short Form 12; QALY = quality-adjusted life year; D6 = Diabetes 6; UMD=Unadjusted mean difference; AMD=adjusted mean difference. *Intervention minus control. Comparisons include clustering for nurse. **Intervention minus control. Cost comparisons account for clustering for nurse plus covariates for baseline cost, age, gender, marital status, ethnicity, duration of diabetes and baseline utility. QALY comparisons account for clustering for nurse plus covariates for age, gender, marital status, ethnicity, duration of diabetes and baseline utility.										

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Table 4. Group comparison for fidelity to MI and CBT.			
MI domain ^a	D6	Standard care	<i>p</i> -value*
Global Spirit	3.23 (1.13)	2.87 (0.87)	0.14
Global Empathy	3.00 (2.00–4.00)	2.50 (2.00–3.00)	0.19
Proportion Complex Reflections	0.35 (0.20)	0.40 (0.17)	0.25
Proportion Open Questions	0.36 (0.17)	0.25 (0.10)	<0.01
Reflection/Question Ratio	0.57 (0.47–0.72)	0.74 (0.53–1.19)	0.03
Proportion Motivational Interviewing Adherent	0.58 (0.32)	0.54 (0.28)	0.51
CBT skills			
BECCI score	1.33 (0.56)	1.12 (0.55)	0.12
Data are mean (standard deviation), or median (interquartile range), as appropriate. MI=Motivational interviewing; CBT=Cognitive behaviour therapy; D6=Diabetes 6; BECCI=Behaviour Change Counselling Index. *Based on result of either a t-test or Mann-Whitney U-test. ^a The MITI guidance indicates that to reach proficiency, a practitioner must achieve an average global spirit rating of 3.5, a reflection to question ratio of ≥ 1 , ≥ 0.5 open questions relative to all questions, ≥ 0.4 complex reflections relative to all reflections, and ≥ 0.9 MI adherent.			

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573 **Appendices**

574 Appendices to: Cluster randomised controlled trial of a psychological intervention for type 2
575 diabetes.

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590 **1 Full description of the study's methods**

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592 **Trial design**

593 D6 was a pragmatic parallel two-arm cluster RCT design for 18 months. Ethical approval was
594 granted by the King's College Hospital Research Ethics Committee (reference 09/H0808/97)
595 and by the respective Primary Care Trusts (reference RDLSLBex 534 and 2010/403/W).
596 Changes to the protocol were approved by the Trial Steering Committee and the Research
597 Ethics Committee. All participants gave informed consent, including access to their medical
598 records.

599 All moderate-to-large GP practices (≥ 6000 patients registered) in the Lambeth, Southwark,
600 Lewisham, Wandsworth, and Bexley Clinical Commissioning Groups, representing a resident
601 population of 1.43 million in south London, UK, were invited to participate if they had a
602 practice nurse delivering diabetes care. Practices were reimbursed £10k for seconding their
603 nurse for one day/week for 15 months. We began recruiting patients after each practice
604 consented to randomisation. The study was conducted in two phases as recruitment had
605 slowed down significantly secondary to organisational uncertainties caused by the Health and
606 Social Care Act 2012. This Act reorganised the UK's National Health Service (NHS),
607 dismantling current organisational structures and creating new ones for funding,
608 management, accountability, and regulation.¹⁵

609 **Patients**

610 The target population was adults with T2D who had persistent suboptimal glycaemic control
611 despite care pathways based on national guidance,¹⁷ therefore a group likely to have barriers
612 to achieving optimal self-management. The study population was patients on diabetes
613 registers of consenting practices. Using standardised search strategies, a list of potentially
614 eligible patients based on the HbA1c (current and preceding 18 months) was generated by
615 each practice and invited to participate. Three practices were eligible and willing to
616 participate but did not have a nurse to second. A protocol change was made in Phase 2, which
617 allowed a consenting practice without a nurse to amalgamate with an adjacent consenting
618 practice which had a nurse, and each pair formed one cluster. The rationale was that the

patient catchment area was likely to be similar and that both practices used the same clinical guidance for diabetes care.

Inclusion criteria were adults aged 18–79 years, duration of T2D for ≥ 2 years, persistent suboptimal glycaemic control defined as HbA1c ≥ 69.4 mmol/mol on two occasions (at least once in the preceding 18 months and at recruitment) while on at least two oral diabetes medications (metformin and one other), and/or requiring insulin therapy. The HbA1c was lowered to ≥ 64 mmol/mol in Phase 2 to increase recruitment. These lower cut-offs for HbA1c was selected to maximise the proportion of patients who could potentially benefit. The minimum requirement of being prescribed at least two classes of oral diabetes medications was to ensure that efforts to optimise and intensify medical care according to national guidance had been offered to the patient before randomisation. Exclusion criteria were: severe mental disorders; terminal illnesses and end-stage diabetes complications; morbid obesity with a BMI >40 kg/m² in Phase 1, which was raised to >50 kg/m² in Phase 2 to enhance recruitment; non-ambulatory as patients had to be able to attend the clinic; no phone/internet access; non-English-speaking as therapy was delivered in English; and currently receiving psychological treatments from elsewhere. Patients who had Patient Health Questionnaire-9 (PHQ-9) depressive scores >20 were excluded if they had psychotic depression or active suicidal ideation.¹⁶

Randomisation

Randomisation of practices (unit of cluster) was conducted after baseline data were collected by an independent statistician using a random number generator to assign equal numbers of practices to each arm at each phase. Allocation concealment was conducted by holding the randomisation list by an independent manager in password-locked computer. The trial manager was only able to reveal to themselves, and then to one D6 researcher, the allocation after entering the details of the practice.

Randomisation of clusters was intended to take place after all the patients had been recruited but this was leading to unacceptable delays in training the nurses. Therefore, some patients were recruited after randomisation of clusters but remained blind to allocation until the interventions were offered in both groups.

Procedures

Baseline measures

Baselines measures were: age, gender, self-reported ethnicity, occupation, employment status, and smoking status. HbA1c was measured centrally (King's College Hospital NHS Foundation Trust) by affinity chromatography (Primus Ultra2, Kansas City, USA) and reported in mmol/mol. Complication status was assessed before randomisation by the research assistant as follows: neuropathic ulcer risk was assessed by perception of 10g monofilament; retinopathy coding was taken from the most recent of annual standardised digital retinal photography documented in the community-based Diabetic Eye Complications Screening Service (DECS), with a new appointment arranged if one had been missed; urine was collected to assess nephropathy using the urinary albumin:creatinine ratio (ACR); and history of macrovascular complications collected from the medical records.

In addition, the following secondary outcomes were measured: systolic and diastolic blood pressure using an electronic sphygmomanometer; body mass index (BMI) (kg/m^2) and waist circumference (cm); depressive symptoms using the Patient Health Questionnaire-9 questionnaire;¹⁶ the Alcohol Use Disorders Identification Test (AUDIT);²³ and the Diabetes Distress Scale, which measures diabetes specific psychological burden (in the protocol we had proposed a similar but longer scale).²⁴ A fasting blood sample was sent for measurement of HbA1c, total cholesterol, and triglycerides.

Intervention

Group 1: Standard care

The nurse delivered diabetes care in both groups as recommended by national guidance.¹⁷ To control for attention, standard care nurses offered the same number of sessions as in D6. The sessions were audio-taped for assessment of contamination bias.

Group 2: Standard care plus D6

D6 aimed to provide the nurses with skills based on MI and CBT to address psychological barriers maintaining poor self-management. The theory underlying MI is that the patient's state of ambivalence (resistance versus willingness to make lifestyle changes) is the core psychological construct that needs addressing.⁶ MI is a directive, person-centered counselling style which encourages patients to change behaviours using collaborative, non-judgmental, and affirming communications. The theory underlying CBT is that barriers to diabetes self-

management are maintained by unhelpful thoughts (e.g., *if I can't cure diabetes, what's the point?*), unhelpful behaviours (e.g., missing insulin doses), and distressing emotions (e.g., low mood/anxiety when seeing a high blood glucose reading).^{18,19} Identifying and challenging these cognitive barriers are effective in changing behaviours.²⁰

The D6 nurses were trained in six skills drawn from MI and CBT: 1. Active listening; 2. Managing resistance; 3. Directing change; 4. Supporting self-efficacy; 5. Addressing health beliefs; and, 6. Shaping behaviours. These skills were applied to common barriers around diabetes such as medication adherence, self-testing, physical activity and dietary changes. The training was conducted by a senior diabetes-experienced clinical psychologist and lasted three months. It comprised three hours per week, interactive classroom activities, a training caseload (average 3-5 non-study patients), and weekly supervision of audiotaped sessions. We produced a manual containing the rationale for D6, the six psychological skills, case examples, strategies to manage clinician's own resistance, and for 'troubleshooting' common clinical obstacles. D6 nurses were expected to apply the skills flexibly to different situations (e.g., weight loss, medication adherence) using visual aids and worksheets. The format was 12 face-to-face individual sessions (sessions 1-4 fortnightly during months 1-2, sessions 5-6 monthly during months 3-6, and sessions 7-12 during months 7-12). Monthly group supervision by a senior clinical psychologist was provided. The sessions were audio-taped for assessment of fidelity.

The Motivational Interviewing Treatment Integrity (MITI) Scale (version 3.1.1)²¹ and Behaviour Change Counselling Index (BECCI)²² were used to assess treatment fidelity of D6, and to compare competencies in both groups. The MITI assesses: global spirit and global empathy with scores ≥ 3.5 (range 1-5); percentage of complex reflections, open questions, and MI adherent behaviours with scores of $\geq 40\%$, 50% , and 90% respectively; and ratio of reflections to closed questions scores with ≥ 1 as proficient. The middle 20 minutes of sessions were rated by two independent psychologists trained in MITI and blind to treatment allocation. The BECCI consists of 11 items with 5-point Likert scales to rate the frequency or the strength of the nurse skill, ranging from 0 (not at all) to 4 (a great extent). A clinical psychologist, blind to treatment allocation, rated the BECCI. We stratified sessions by nurse and patient and then randomly selected tapes (that lasted ≥ 20 minutes) for 3 different patients for each nurse from either session 2, 3 and 4. Three nurses did not have three tapes lasting 20 minutes or more and, for these, the three longest tapes were chosen.

Outcomes

As the recruitment and follow-up was delayed by the NHS restructuring and patient attrition, the protocol was changed from 24 months follow-up to 18 months. The primary outcome was change in HbA1c from cluster randomisation to 18 months. If the study HbA1c data were missing at 18-month, we used routinely collected HbA1c data if it was collected within the 15-month follow-up window. Secondary outcomes were change in lipids, blood pressure, BMI and depressive symptoms at 18 months. Research assistants were blind to allocation when collecting follow-up data.

Sample size

A 10.9 mmol/mol difference in HbA1c in D6 compared to standard care was the minimal clinically acceptable reduction at 18 months, considering: (a) baseline HbA1c and (b) that standard care may produce a 2.2 mmol/mol (equivalent to 0.2%) reduction in HbA1c for the placebo effect of participating in a RCT (actual difference between groups 8.8 mmol/mol (equivalent to 0.8%), equivalent to a moderate effect size of $d=0.55$). Assuming 20% dropout, we needed 360 patients to achieve 80% power at a two-sided alpha-level of 5%, with 20 practices with 18 patients each per arm. We then took account of clustering by practice and we assumed two practices per arm dropped out. Therefore, we needed 24 practices with a total patient size of $24 \times 18 = 432$ patients. The required sample size adjusted for a clustering intra-correlation coefficient (ICC) effect of 0.05 was $81 \times 1.7 = 138$ patients per arm (inflation factor 1.7).

We recruited 334 patients of which 231 had at least one follow-up in 24 clusters. The average cluster size was therefore 10 patients per cluster, smaller than our assumed size of 15 patients per cluster with a post-hoc power of 77% (STATA 13 *clsampsi* function) at two-sided alpha-level of 5%.²⁵

Statistical analysis

Data were analysed using STATA 13. The sample characteristics were described as means (standard deviation (SD)) or as proportions (percentage). A comparison of patient list size and Index of Multiple Deprivation rank score by practices that participated versus those that did not was conducted using Student's t-test.²⁶ A linear mixed-effects model estimated group differences in HbA1c levels between D6 and standard care groups at 18 months. We included

the 15-month HbA1c as this clinically just overlaps with the 3-month window for 18-month HbA1c and to include more patients with at least one follow-up measure. Data were analysed as intention-to-treat (ITT). Time (with two levels: 15 and 18 months), treatment group, an interaction between treatment group and time, Primary Care Trust (as a possible prognostic factor), recruitment phase, and baseline HbA1c were included as fixed covariates. The dependency of the repeated observations of the same subjects was modeled on the covariance between the residuals using an unstructured covariance pattern model. Nurse was included as a random effect as the unit of randomisation.

Observations from the same nurse cluster were likely to be more similar than observations from two different clusters. However, in three cases, a practice was twinned with an adjacent practice and one nurse covered both practices. Therefore, two types of clustering could occur: within practice and within nurse. We assumed that nurse clustering would have a stronger effect than practice clustering. We therefore treated the twinned practices as one unit which is equivalent to treating nurse as the primary clustering unit. However, we repeated the model using ‘practice’ as the main clustering unit in a sensitivity analysis.

Secondary outcomes were analysed in the same way using linear mixed models to estimate group differences at 18 months (including 15 months). An independent covariance structure pattern was used for the triglycerides as the model did not converge using unstructured covariance.

Twenty-nine participants with HbA1c <64 mmol/mol contrary to the study criteria were included and this was a protocol violation. We performed a sensitivity analysis by including a binary covariate of this protocol violation (yes/no) in the model.

The analyses were conducted using maximum likelihood under the missing at random assumption. Sensitivity analyses were carried out to assess sensitivity to missingness in HbA1c using several approaches: by investigating and including predictors of missingness in the model and by using multiple imputation for the missing values of HbA1c (50 imputations using *mi* impute command in STATA 13 with all variables from the mixed-effects model included in the imputation model, as well as age, ethnicity, gender, baseline BMI, total cholesterol, triglycerides, blood pressure, and PHQ-9 score).

The Data Monitoring Committee oversaw the study.

771 **Fidelity**

772 To assess IRR for each fidelity measure, absolute agreement was measured by estimating the
773 ICC from a two-way mixed model or using Spearman's rank correlation coefficient if
774 residuals from the mixed model were not normally distributed. A t-test or Mann-Whitney U-
775 test was used to compare the skills of D6 versus standard care nurses, using STATA 14.

776 **Role of funding source**

777 The funder of the study had no role in study design, data collection, data analysis, data
778 interpretation, or reporting. The authors had full access to all data and final responsibility for
779 submission for publication and acted independently from the funding source.

780 **Patient Involvement**

781 We included a person with type 1 diabetes from our local community who also was an active
782 member of the local and national Diabetes UK. This person was instrumental in guiding us
783 to use NHS practice nurses rather than research diabetes nurses to deliver the intervention.
784 This person inputted into the importance of quality of life and psychological well-being as
785 outcome measures alongside glycaemic control. For the process evaluation, we invited
786 participants to give us feedback of the intervention in terms of the perception of burden as
787 patients. We included a person with type 1 diabetes on the Trial Steering Committee.

788 **Transparency Declaration**

789 The lead author affirms that the manuscript is an honest, accurate, and transparent account of
790 the study being reported; that no important aspects of the study have been omitted; there were
791 discrepancies from the study as planned and these have been explained.

2 Additional Tables

Table 1. Breakdown of patients attending each practice and primary outcome follow-up rates by group.			
D6		Standard care	
Practice*	Proportion with HbA1c data at 18 months (%)	Practice*	Proportion with HbA1c data at 18 months (%)
1	14/18 (77.8)	2	11/12 (91.7)
3	13/19 (72.2)	4	14/19 (73.7)
5	7/16(64.3)	6	11/18 (61.1)
7	6/9 (66.7)	8	12/17 (70.6)
9	15/16 (93.8)	10	6/12 (50.0)
11	6/12 (50.0)	12	13/13 (100.0)
13	6/9 (66.7)	14	13/17 (76.5)
15**	9/18 (50.0)	16	13/17 (76.5)
17	9/13 (69.2)	18	5/8 (62.5)
19**	12/14 (85.7)	20***	1/4 (25.0)
21	8/14 (57.1)	22	5/11 (45.5)
23**	4/12 (33.3)	24	6/16 (37.5)
Total	109/170 (64.1%)	Total	110/164 (67.1%)
<p>* Practices 1-6 are from Phase 1 (HbA1c \geq 69.4 mmol/mol and BMI \leq 40kg/m²). Practices 7-24 are from Phase 2 (HbA1c \geq 64 mmol/mol, BMI \leq 50kg/m², and twinned practices).</p> <p>** Two practices twinned and covered by 1 nurse.</p> <p>*** Practice dropped out post-randomisation.</p> <p>D6=Diabetes 6</p>			

Table 2. Comparison of missingness in HbA1c at 18 months.			
Variable	HbA1c measured at 18 months (n=219)	Missing HbA1c at 18 months (n=115)	Test of independence (t-test or Pearson χ^2-test)
Age (years)	58.9 (11.4)	59.0 (11.0)	$t=0.045, p=0.964$
Ethnicity			
White	72 (33.0)	62 (54.4)	$\chi^2(3)=14.854, p=0.001$
African/Caribbean	103 (47.3)	40 (35.1)	
Asian/Other	43 (19.7)	12 (10.5)	
Gender			
Male	104 (47.5)	59 (51.3)	$\chi^2(1)=0.439, p=0.507$
Female	115 (52.5)	56 (48.7)	
Education level			
A levels or higher	60 (27.9)	30 (26.6)	$\chi^2(2)=0.091, p=0.956$
O level or GCSE equivalent	75 (34.9)	41 (36.3)	
No formal qualifications	80 (37.2)	42 (37.2)	
Relationship status			
Married or Cohabiting	112 (51.3)	59 (51.3)	$\chi^2(2)=1.221, p=0.543$
Separated/Divorced/Widowed	60 (27.7)	37 (32.2)	
Single	45 (20.7)	19 (16.5)	
Employment			
Yes	92 (42.0)	47 (40.9)	$\chi^2(1)=0.040, p=0.841$
No	127 (58.0)	68 (59.1)	
BMI (kg/m ²)	32.1 (6.0)	31.5 (6.4)	$t=-0.839, p=0.402$
Systolic BP (mm/Hg)	133.6 (17.2)	135.3 (16.9)	$t=-0.823, p=0.411$
Diastolic BP (mm/Hg)	79.2 (10.0)	79.2 (10.3)	$t=-0.052, p=0.958$
HbA1c (mmol/mol)	79.1 (17.4)	83.2 (19.3)	$t=-1.96, p=0.051$
Total Cholesterol (mmol/L)	4.2 (1.1)	4.3 (1.3)	$t=-0.501, p=0.617$
Fasting triglycerides (mmol/L)	1.6 (1.2)	1.9 (1.4)	$t=-1.631, p=0.104$
Diabetes duration (years)	10.5 (6.1)	10.0 (6.7)	$t=-0.694, p=0.488$
DDS (mean item score)	2.2 (0.8)	2.3 (0.8)	$t=0.959, p=0.338$
Data are n (%) or mean (SD), as appropriate.			
¹ Yes = full time, part-time, student or self-employed			
² No = retired/unemployed/not seeking employment			
BMI = Body mass index; BP = blood pressure; DDS = Diabetes Distress Scale			

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Table 3. Inter-rater reliability for each MI domain.	
MI Domain	Inter-rater reliability*
Global Spirit (ICC)	0·87
Global Empathy (Spearman's rho)	0·91
% Complex Reflections (ICC)	0·86
% Open Questions (ICC)	0·92
Reflection/Question Ratio (Spearman's rho)	0·88
% MI Adherent (ICC)	0·90
MI=Motivational interviewing; ICC=Intra-class correlation coefficient *Reliability was calculated as an ICC if the distribution was normal and a Spearman's rho if non-normal.	

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800 We rated 69 sessions (4.0% of all available recordings) for fidelity from 33/170 and 36/164
 801 patients from the D6 and standard care groups, respectively. The level of competency in the
 802 D6 group was below the beginner proficiency level in all the scales for MI and BECCI.
 803 Except for a slightly higher proportion of open questions in D6, and a slightly larger
 804 reflection/question ratio in standard care, there were no statistically significant differences in
 805 the remaining mean MI domain scores or BECCI scores.

[illegible]

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810 **3 CONSORT 2010 checklist of information for reporting a cluster randomised**
811 **trial**

Section/Topic	Item No	Standard Checklist item	Extension for cluster designs	Page No *
Title and abstract				
	1a	Identification as a randomised trial in the title	Identification as a cluster randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts) ^{i,ii}	See table 2	2
Introduction				
Background and objectives	2a	Scientific background and explanation of rationale	Rationale for using a cluster design	4-5
	2b	Specific objectives or hypotheses	Whether objectives pertain to the the cluster level, the individual participant level or both	4
Methods				
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	Definition of cluster and description of how the design features apply to the clusters	5-6
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons		Appendix
Participants	4a	Eligibility criteria for participants	Eligibility criteria for clusters	5
	4b	Settings and locations where the data were collected		5
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	Whether interventions pertain to the cluster level, the individual participant level or both	6-7
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	Whether outcome measures pertain to the cluster level, the individual participant level or both	7-8
	6b	Any changes to trial outcomes after the trial commenced, with reasons		7-8, Appendix
Sample size	7a	How sample size was determined	Method of calculation, number of clusters(s) (and whether equal or unequal cluster sizes are assumed), cluster size, a coefficient of intracluster correlation (ICC or k), and an indication of its uncertainty	8, Appendix
	7b	When applicable,		NA

		explanation of any interim analyses and stopping guidelines	
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	6, Appendix
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	6, Appendix
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	6, Appendix
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	Replace by 10a, 10b and 10c
	10a		Who generated the random allocation sequence, who enrolled clusters, and who assigned clusters to interventions
	10b		Mechanism by which individual participants were included in clusters for the purposes of the trial (such as complete enumeration, random sampling)
	10c		From whom consent was sought (representatives of the cluster, or individual cluster members, or both), and whether consent was sought before or after randomisation
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	8
	11b	If relevant, description of the similarity of interventions	6-7
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	8-9, Appendix
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	8-9, Appendix

Results				
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	For each group, the numbers of clusters that were randomly assigned, received intended treatment, and were analysed for the primary outcome	9-10, Figure 1, Appendix 3 Table 1
	13b	For each group, losses and exclusions after randomisation, together with reasons	For each group, losses and exclusions for both clusters and individual cluster members	9-10, Figure 1, Appendix 3 Table 1
Recruitment	14a	Dates defining the periods of recruitment and follow-up		Figure 1, Appendix
	14b	Why the trial ended or was stopped		NA
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Baseline characteristics for the individual and cluster levels as applicable for each group	Table 1
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	For each group, number of clusters included in each analysis	10, Figure 1
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Results at the individual or cluster level as applicable and a coefficient of intracluster correlation (ICC or κ) for each primary outcome	10-11
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended		NA
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory		10-11, Appendix
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms ⁱⁱⁱ)		12
Discussion				
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses		12-15
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	Generalisability to clusters and/or individual participants (as relevant)	12-15
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant		12-15

evidence			
Other information			
Registration	23	Registration number and name of trial registry	2
Protocol	24	Where the full trial protocol can be accessed, if available	NA
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	17

** Note: page numbers optional depending on journal requirements*

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4 Supplementary Data from the Economic Evaluation

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4.1 Summary of methods

A within-trial economic evaluation assessed the cost-effectiveness of D6 from a health and social care perspective at 18 months. This linked individual-level costs with HbA1c and quality-adjusted life year (QALY) gains estimated from the Short Form 12 (SF-12) version 2.^{52,53} We calculated individual-level total costs (English pounds sterling, £, 2011–12 prices) by attaching unit costs from national sources to individual-level (all-cause) resource use quantities covering a retrospective 6-month period at baseline and 18 months. Use of hospital services was assessed by retrospective review of hospital records. Use of out-of-area hospital services, community-based services, and medications were measured by self-report using a specifically developed proforma. Cost estimates for D6 included the full costs of staff training/supervision/assessment and time spent on delivery to patients. Outcomes and costs at 18 months were discounted by 3.5%.

Costs and QALY gains at 18 months were compared using non-parametric bootstrap regressions (10000 repetitions) with baseline covariates and adjustment for nurse. We only calculated incremental cost-effectiveness ratios where either group showed statistically greater costs and outcomes. The probability of cost-effectiveness for D6 was assessed by constructing cost-effectiveness acceptability curves (10000 bootstrap repetitions) for threshold ranges of £0–£50,000 per QALY gain/point improvement in HbA1c. Sensitivity analyses explored the impact on cost and/or outcome differences when: (a) missing data due to loss of follow-up were imputed (using multiple imputation in STATA 11.2) rather than excluded, (b) the unit cost of the D6 intervention was lowered by assuming 50% more people received D6, (c) accounting for the inadvertent inclusion of 29 individuals with HbA1c <64 mmol/mol by including a binary covariate for this, and (d) accounting for clustering at practice rather than nurse level.

4.2 Intervention Costs

Table S1: D6 intervention costs (English pounds sterling, £, 2011–12 prices; total costs rounded to nearest £)

Intervention Component	Description	Resources	Resource and cost details	Total cost	Unit cost per participant (n164)
Training	One training session (three hours) per week for 12 weeks, for 11 trainees. Delivered by one clinical psychologist over two training courses.	Trainer's time	1 band 8a clinical psychologist for 4 hours (3 hour training plus 1 hour preparation) for 12 weeks for 2 courses (1 * 4 * 12 * 2 * £60 ¹) £5,760	£20,074	£122
		Trainees' time	11 trainees (primary care nurses) for 3 hours for 12 weeks (11 * 3 * 12 * £35 ²) £13,860.		
		Capital/materials	Room to train in: 3 hours training for 12 weeks for 2 courses (3 * 12 * 2 * £3.10 per hour ³) £223.20. Printing of 11 D6 psychology skills handbook: (11 * £11.94 ⁴) £131.34. Printing of 10 A4 PowerPoint presentations for 12 session for 11 trainees (10 * 12 * 11 * £0.06 ⁵) £79.20. Use of 1 video camera: £19.99 ⁶		
Supervision	Supervision for trainees provided in two hour group sessions by a clinical psychologist.	Trainer's time	1 band 8a clinical psychologist for 3 hours (2 hour supervision plus 1 hour preparation) for a total of 35 group supervision sessions (1 * 3 * 35 * £60 ¹) £6,300. 1 band 8a clinical psychologist for 30 minutes for transcription of 131 taped trainee sessions (0.5 * 131 * £60 ¹) £3,930.	£23,449	£143
		Trainees' time	1 trainee (primary care nurse) for 2 hours for 140 trainee attendances at group sessions (1 * 2 * 140 * £35 ²) £9,800.		
		Transcription	Transcription of 131 30-minute sessions: (131 * 30 * 0.80) £3,144 ⁷ .		
		Materials	1 audio recorder per trainee: (11 * £24.99 ⁸) £274.89.		
Assessment	One 30-minute assessment by band 8a nurse per trainee	Assessor's time	1 band 8a nurse for 30-minutes, for 11 assessments (1 * 0.5 * 11 * £60 ⁹) £330	£330	£2

Total for training				£43,853	£267
Intervention	Participants offered 12 sessions over twelve months.	Trainees' time	Individually calculated for each case based on number of sessions attended (assume 30 minute session): (30 minutes * £0.75 per minute ¹⁰) £22.50 per session.	Cost per patient	Mean £301
Sources and details (all pounds sterling (£), 2011/12 prices):					
1. Curtis L. 2012. Unit Costs of Health and Social Care 2012. Personal Social Services Research Unit: University of Kent. Based on £60 per hour, band 8a clinical psychologist.					
2. Curtis L. 2012. Unit Costs of Health and Social Care 2012. Personal Social Services Research Unit: University of Kent. Based on £35 per hour excluding qualifications.					
3. Hurley MV, Walsh NE, Mitchell HL, Pimm J, Williamson E, Jones RH, Reeves BC, Dieppe PA, Patel A. Economic evaluation of a rehabilitation program integrating exercise, self-management, and active coping strategies for chronic knee pain. Arthritis & Rheumatism (Arthritis Care & Research) 2007; 57 (7): 1220-1222. Obtained further details via correspondence with the authors. Based on capital costs of a gym (£5.10 per hour, 2003/4 prices), halved to give more appropriate sized room (£2.55), inflated to 2011/12 prices (£3.10), (inflation source: Curtis L. 2012. Unit Costs of Health and Social Care 2012. Personal Social Services Research Unit: University of Kent, The Hospital & Community Health Services (HCHS) index – annual percentage prices increase).					
4. Information from the clinical team: £11.94 each.					
5. Rymans photocopying. Available at: http://www.ryman.co.uk/photocopying [accessed: 13/02/2015]: £0.06 per copy for 100+ pages					
6. Argos camcorder. Available at: http://www.argos.co.uk/static/Product/partNumber/2268077.htm [accessed: 13/02/2015]: £19.99 for the lowest priced camcorder.					
7. Transcript Divas Transcription Services. Available at: http://transcriptdivas.co.uk/ [accessed: 13/02/15] Based on £0.80 per minute of recording data.					
8. Argos voice recorder. Available at: http://www.argos.co.uk/static/Product/partNumber/3071452.htm [accessed: 13/02/2015]: £24.99 for the lowest priced voice recorder.					
9. Curtis L. 2012. Unit Costs of Health and Social Care 2012. Personal Social Services Research Unit: University of Kent. Based on £46,600 median full-time equivalent total earnings for a band 8a nurse, with proportions of a band 7 nurse for per hour cost applied (£40,200 - £52 per hour): £60 per hour.					
10. Curtis L. 2012. Unit Costs of Health and Social Care 2012. Personal Social Services Research Unit: University of Kent. Based on £45 per hour of face-to-face contact excluding qualifications.					

846 **4.3 Other Unit Costs**

847 **Table S2: Unit costs**

Item	Unit	Unit cost (£) 2011-12 prices	Source	Notes
Inpatient services				
Nervous System	bed day	368	1	NHS reference cost - Code A
Eyes & Periorbital	bed day	606	1	NHS reference cost - Code B
Mouth, head, neck & ears	bed day	519	1	NHS reference cost - Code C
Respiratory system	bed day	326	1	NHS reference cost - Code D
Cardiac Surgery & Primary Cardiac Conditions	bed day	452	1	NHS reference cost - Code E
Digestive System	bed day	428	1	NHS reference cost - Code F
Hepato-biliary and Pancreatic Systems	bed day	398	1	NHS reference cost - Code G
Musculoskeletal System	bed day	486	1	NHS reference cost - Code H
Skin, Breast & Burns	bed day	404	1	NHS reference cost - Code J
Endocrine & Metabolic System	bed day	327	1	NHS reference cost - Code K
Urinary Tract & Male Reproductive Systems	bed day	350	1	NHS reference cost - Code L
Female Reproductive System & Assisted Reproduction	bed day	599	1	NHS reference cost - Code M
Obstetrics	bed day	818	1	NHS reference cost - Code N
Diseases of Childhood & Neonates	bed day	577	1	NHS reference cost - Code P
Vascular System	bed day	472	1	NHS reference cost - Code Q
Radiology and Nuclear Medicine	bed day	513	1	NHS reference cost - Code R
Haematology, Chemotherapy, Radiotherapy & Specialist Palliative Care	bed day	448	1	NHS reference cost - Code S
Multiple Trauma, Emergency Medicine and Rehabilitation	bed day	458	1	NHS reference cost - Code T
Immunology, Infectious Diseases & other contacts	bed day	360	1	NHS reference cost - Code W
General inpatient	bed day	439	1	NHS reference cost - Overall inpatient
A&E	bed day	112	1	TAandEMSNA - Accident and Emergency Services: Not Leading to Admitted
Outpatient services				
Diabetes clinic	visit	134	1	307 - diabetic medicine on Total-OPATT tab
Diabetes foot clinic	visit	134	1	cost as diabetes clinic
Diabetes eye clinic	visit	134	1	cost as diabetes clinic
Ophthalmology	visit	86	1	130 - ophthalmology on Total-OPATT tab
Blood tests / phlebotomy	visit	3	1	DAP839 - Phlebotomy: on TDAPS tab (Pathology services)
Dietetics	visit	57	1	Total - OPATT Tab: Service code 654A - Adult dietetics
General medical outpatient	visit	158	1	300 - general medicine on Total-OPATT tab
Day surgery centre	visit	123	1	Total OPATT (Outpatient Attendances Data) tab - code 100 - general surgery
A&E	visit	110	1	180 - A&E on Total-OPATT tab
X-ray (x-ray only)	visit	30	1	Total - OPATT Tab: Direct Access Plain Film - DAPF
Community based professionals				
GP at surgery	contact	36	2	P183 - PSSRU - per patient contact lasting 11.7 minutes - Excludes qualification costs, including direct care staff costs.
GP at home	contact	92	2	P183 - PSSRU - per patient out of surgery visit lasting 23.4 minutes - Excludes qualification costs, including direct care staff costs.
GP telephone	contact	22	2	P183 - PSSRU - per telephone contact lasting 7.2 minutes - Excludes qualification costs, including direct care staff costs.
Diabetes specialist nurse at surgery	contact	11.11	2	p178 - PSSRU - Nurse specialist - £43 per hour excluding qualifications, assuming 15.5 (specified on p180 for practice nurse) min appointment
Diabetes specialist nurse at home	contact	16.11	2	p178 - PSSRU - Nurse specialist - £43 per hour excluding qualifications, - using per hour of home visiting from community nurse (p175) - £61:£42 = 1.45 SO - 11.11*1.45=16.11
Diabetes specialist nurse telephone	contact	6.78	2	p178 - PSSRU - Nurse specialist - £43 per hour

					excluding qualifications, assume same proportion of costs as a GP telephone call (61% (*0.61)) - $11.11 * 0.61 = 6.78$
Practice nurse at surgery	contact	11.63	2		P180 - PSSRU - £45 per hour of face-to-face contact excluding qualifications assuming 15.5 (specified on p180) min appointment
Practice nurse at home	contact	16.166	2		based on practice nurse surgery visit cost above but use the proportion of district nurse home visit hour / clinic hour proportion from PSSRU 2010 ($68/49=139\%$)
Practice nurse telephone	contact	7.0943	2		assume same proportion of costs as a GP telephone call (61% (*0.61))
Chiropodist/podiatrist at surgery	contact	48.529	1		TOCS tab - N910 Podiatry services - £47 per activity
Chiropodist/podiatrist at home	contact	70.367	1		TOCS tab - N910 Podiatry services - £47 per activity - with proportions of home visit from community nurse (p175, PSSRU) - $£61 : £42 = 1.45$ SO - $47 * 1.45 = 68.15$
Chiropodist/podiatrist telephone	contact	29.603	1		assume same proportion of costs as a GP telephone call (61% (*0.61))
Optician at surgery	contact	20.7	3		"The fee paid to an optical contractor for carrying out an NHS sight test by the governments of England, Wales, and Northern Ireland remains at £20.70 for the year 1 April 2011 to 31 March 2012"
Optician at home	contact	28.773	2		based on surgery visit cost above but use the proportion of district nurse home visit hour / clinic hour proportion from PSSRU 2010 ($68/49=139\%$)
Optician telephone	contact	12.627	2		assume same proportion of costs as a GP telephone call (61% (*0.61))
District nurse at surgery	contact	11.347	2		based on district nurse home visit cost above but use the proportion of clinic hour / home visit hour proportion from PSSRU 2010 ($49/68=72\%$)
District nurse at home	contact	15.76	2		P175 - PSSRU - Community nurse including district - £61 per hour of home visiting including travel, excluding quals, assume 15.5 (see page 180) min appointment
District nurse telephone	contact	9.6136	2		assume same proportion of costs as a GP telephone call (61% (*0.61))
Dietician at surgery	contact	72.277	1		TOCS tab - N800 Dietetics services - £70 per activity
Dietician at home	contact	104.8	1		Cost combines price from 2011/12 (above) but with proportions of home visit from community nurse (p175, PSSRU) - $£61 : £42 = 1.45$ SO - $70 * 1.45 = 101.5$
Dietician telephone	contact	44.089	1		assume same proportion of costs as a GP telephone call (61% (*0.61))
Physiotherapist at surgery	contact	48.529	1		TCSCCT tab (community based therapy services) - N5A1 - Community Physiotherapy Services : Adult - One-to-One Services - £47
Physiotherapist at home	contact	70.367	1		TCSCCT tab (community based therapy services) - N5A1 - Community Physiotherapy Services : Adult - One-to-One Services - £47 - but with proportions of home visit from community nurse (p175, PSSRU) - $£61 : £42 = 1.45$ SO - $47 * 1.45 = 68.15$
Physiotherapist telephone	contact	29.603	1		assume same proportion of costs as a GP telephone call (61% (*0.61))
Occupational therapist at surgery	contact	30	2		p168 - pssru - NHS community OT - £30 per hour - assume 1 hour meeting, Excludes qualification costs.
Occupational therapist at home	contact	54.78	2		Cost combines price from 2011/12 (above) but with proportions of client time set down in 2009-10 (p152) book (£42 per home visit / £23 per hour = 182.61%). £30 per hour (excluding qualifications) multiplied by 182.61%
Occupational therapist telephone	contact	18.3	2		assume same proportion of costs as a GP telephone call (61% (*0.61))
Psychiatrist at surgery	contact	171.4	1		TMHCSOPFUAF tab (Mental Health Consultant Services (Outpatient Setting) - Follow-up Attendance Face to Face) - MHOPFUA2 (Adult other services)
Psychiatrist at home	contact	248.53	1		based on psychiatrist visit cost above but use the proportion of home visiting from community nurse (p175, PSSRU) - $£61 : £42 = 1.45$ SO - $166 * 1.45 = 240.70$
Psychiatrist telephone	contact	51.626	1		TMHCSOPFUANF tab (Mental Health Consultant

Psychologist at surgery	contact	136	2	Services (Outpatient Setting) - Follow-up Attendance Non Face to Face) - MHOPFUA2 (Adult other services) p171 PSSRU - £136 per hour of client contact - assume 1 hour appointment, Excludes qualification costs.
Psychologist at home	contact	189.04	2	based on psychologist visit cost above but use the proportion of district nurse home visit hour / clinic hour proportion from PSSRU 2010 (68/49=139%)
Psychologist telephone	contact	40.8	2	assume same proportion of costs as a psychiatrist face to face v non face to face (30% (*0.30))
Psychotherapist at surgery	contact	136	2	Assume same as a psychologist. "A psychotherapist may be a psychiatrist, social worker, psychologist, mental health nurse or other mental health professional who has had further specialist training in psychotherapy. Increasingly, there are a number of psychotherapists who do not have backgrounds in these fields but who have undertaken in-depth training in this area.
Psychotherapist at home	contact	189.04	2	" - from http://www.nhscareers.nhs.uk/explore-by-career/psychological-therapies/careers-in-psychological-therapies/psychotherapist/ - accessed 16April2013 based on psychotherapist visit cost above but use the proportion of district nurse home visit hour / clinic hour proportion from PSSRU 2010 (68/49=139%)
Psychotherapist telephone	contact	40.8	2	assume same proportion of costs as a psychiatrist face to face v non face to face (30% (*0.30))
Counsellor at surgery	contact	59	2	P53 Pssru - £59 per consultation
Counsellor at home	contact	82.01	2	based on surgery visit cost above but use the proportion of district nurse home visit hour / clinic hour proportion from PSSRU 2010 (68/49=139%)
Counsellor telephone	contact	35.99	2	assume same proportion of costs as a GP telephone call (61% (*0.61))
Social worker at surgery	contact	78	2	P190 - PSSRU - social worker adult services - £156 per hour of face to face contact - assume 30 min appointment - excludes qualifications.
Social worker at home	contact	108.42	2	based on social worker visit cost above but use the proportion of district nurse home visit hour / clinic hour proportion from PSSRU 2010 (68/49=139%)
Social worker telephone	contact	23.4	2	assume same proportion of costs as a psychiatrist face to face v non face to face (30% (*0.30))
Home help/ care worker at surgery	contact	11.58	2	same as surgery
Home help/ care worker at home	contact	11.58	2	P193 PSSRU - Home care worker per hour of face to face contact, Weighted average accounting for different rates for day/evening/weekday/weekends. Plus, info that over 50% of visits are for 30 minutes so accounting for this (23.16/2= £11.58)
Home help/ care worker telephone	contact	7.0638	2	assume same proportion of costs as a GP telephone call (61% (*0.61))
Meals on Wheels at surgery	contact	5	2	same as home visit
Meals on Wheels at home	contact	5	2	P125 PSSRU - £6 local authority meal v £4 independent sector cost per day
Meals on Wheels telephone	contact	3.05	2	assume same proportion of costs as a GP telephone call (61% (*0.61))
Pharmacist for advice at surgery	contact	4.17	2	p172 PSSRU - £50 - assume 5 min consultation - Excludes qualification costs.
Pharmacist for advice at home	contact	4.17	2	same as home visit
Pharmacist for advice telephone	contact	4.17	2	Assume same as a pharmacist surgery consult
NHS direct at surgery	contact	22.358	4	cost as telephone
NHS direct at home	contact	22.358	4	cost as telephone
NHS direct telephone	contact	22.358	4	21.02 in 2009/10 so inflate up to 2011/12
Insulin equipment				
Blood glucose monitor / metre	item	12	5	
Blood glucose testing strips	100-pack	30.1	6	per 100: p459 - accu-chek mobile - n100
Insulin pen	item	15.7	6	per 1 pen: p446 - autopen 24
Insulin pump	item	2375	7	
Needle	100-pack	2.79	1	per 100: p447 - hypodermic needle - n100
Syringe	10-pack	1.35	6	per 10; p447 - U100 syringe with needle - 10 needles - 1.35
Finger prick device	200-pack	2.94	6	p446 - unilet eco - 200

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4.4 Sensitivity Analyses

Table S11: Total costs at baseline and 18 months including intervention costs based on sensitivity analyses (2011/12 prices; all 18 month costs except intervention costs discounted)

	Control			Intervention			Unadjusted mean difference ^s	95% C.I.	Adjusted mean difference ^{ss}	95% C.I. ^s
	<i>valid n</i>	<i>Mean £</i>	<i>SD</i>	<i>valid n</i>	<i>Mean £</i>	<i>SD</i>				
Costs at 18 months										
<i>Per protocol</i>										
Health & social care costs including intervention costs	107	1025	573	92	1184	572	159	-39 to 357	151	-32 to 334
<i>GP Clustering</i>										
Health & social care costs including intervention costs	107	1025	573	92	1184	572	159	-39 to 357	150	-30 to 329
<i>Alternative intervention cost</i>										
Health & social care costs including intervention costs	107	1025	573	92	1095	572	70	-128 to 268	61	-123 to 244
<i>Intention to treat</i>										
Health & social care costs including intervention costs – intention to treat	170	1052	497	164	1126	473	74	-42 to 190	107	7 to 207*

^sComparisons include clustering for nurse. ^{ss}Comparisons include clustering for nurse plus covariates for baseline cost, age, gender, marital status, ethnicity, duration of diabetes and baseline utility. * Statistically significant

Table S12: Outcomes at baseline and 18 months interpolated to a six month period to match the cost data based on sensitivity analyses

	Control			Intervention			Unadjusted mean difference ^s	95% C.I.	Adjusted mean difference ^{ss}	95% C.I. ^s
	<i>valid n</i>	<i>Mean £</i>	<i>SD</i>	<i>valid n</i>	<i>Mean £</i>	<i>SD</i>				
Outcomes at 18 months										
<i>Per protocol</i>										
HbA1c (discounted)	109	71.31	19.22	110	71.60	18.11	0.29	-5.40 to 5.98	0.00	-6.08 to 6.09
SF12 based QALY (discounted and interpolated)	48	0.36	0.06	58	0.37	0.06	0.01	-0.01 to 0.03	0.00	-0.01 to 0.02
<i>GP cluster</i>										
HbA1c (discounted)	109	71.31	19.22	110	71.60	18.11	0.29	-5.38 to 5.97	0.66	-5.43 to 6.75
SF12 based QALY (discounted and interpolated)	48	0.36	0.06	58	0.37	0.06	0.01	-0.01 to 0.03	0.00	-0.01 to 0.00
<i>Intention to treat</i>										
HbA1c (discounted)	170	72.16	16.74	164	72.19	15.61	0.02	-4.34 to 4.39	0.47	-4.75 to 3.82
SF12 based QALY (discounted)	170	0.36	0.06	164	0.37	0.06	0.00	-0.01 to 0.02	0.00	-0.00 to 0.01

and interpolated)

862 ^sComparisons include clustering for nurse. ^{ss}Comparisons include clustering for nurse plus covariates for age, gender, marital status, ethnicity, duration of diabetes and

863 baseline utility. * Statistically significant

4.5 Cost-effectiveness

For the economic analysis, 139 (42%) and 85 (25%) participants had the two necessary combinations of cost/HbA1c/covariate and cost/SF-12/covariate data, respectively; characteristics of those with and without data were comparable.

Based on QALYs, probabilities of cost-effectiveness for the D6 group at 18 months did not exceed 35% at the examined willingness to pay thresholds. However, based on HbA1c, probabilities of cost-effectiveness were around 5% at a willingness to pay threshold of £0, rising to (and remaining at) around 65% at thresholds of £5000–£50000. However, willingness to pay for a point improvement in HbA1c is unknown, and such a small improvement is unlikely to be clinically meaningful. Based on QALYs, probabilities of cost-effectiveness for the D6 group at 18 months did not exceed 35% at the examined willingness to pay thresholds. However, based on HbA1c, probabilities of cost-effectiveness were around 5% at a willingness to pay threshold of £0, rising to (and remaining at) around 65% at thresholds of £5000–£50000. However, willingness to pay for a point improvement in HbA1c is unknown, and such a small improvement is unlikely to be clinically meaningful.

Figure S1: Cost-effectiveness plane for HbA1c changes at 18 months from a health & social care perspective

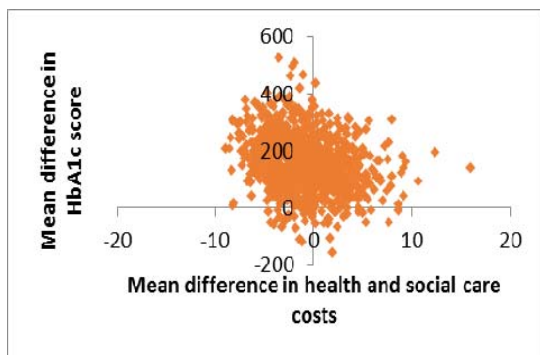


Figure S2: Cost-effectiveness plane for QALY gains at 18 months from a health & social care perspective

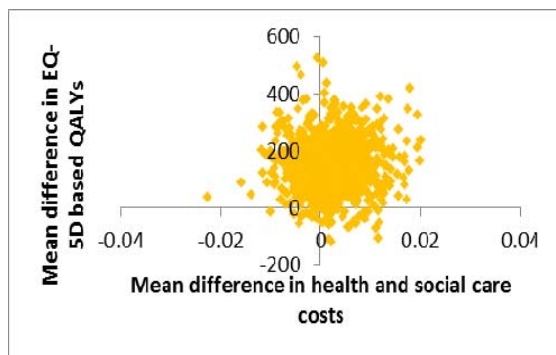


Figure S3: Cost-effectiveness acceptability curve for HbA1c point improvements at 18 months from a health & social care perspective

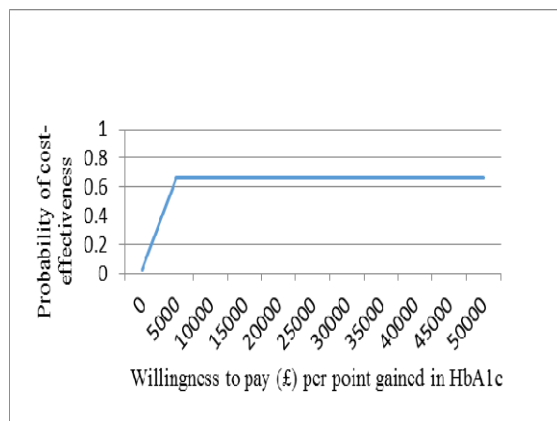
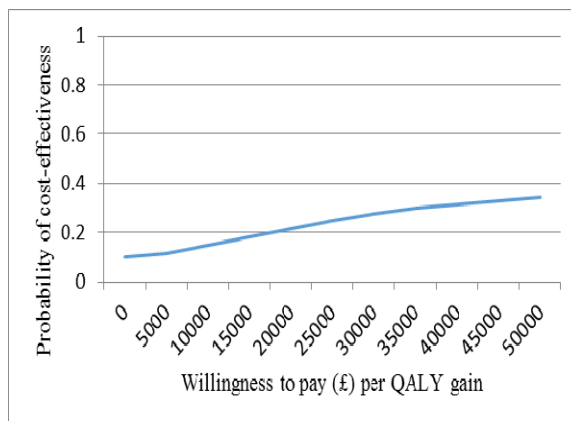


Figure S4: Cost-effectiveness acceptability curve QALY gains at 18 months from a health & social care perspective



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